

# Bayer HealthCare

## Biological Products Division



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April 5, 2004

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852-1448

Carol M. Moore  
Vice President  
Worldwide Regulatory Affairs  
Responsible Head / Agent

Re: Docket No. 2004D-0041  
Comments to Draft Guidance for Industry, "Providing Regulatory  
Submissions in Electronic Format – Content of Labeling"

Bayer HealthCare LLC, Biological Products Division (Bayer BP) has reviewed the Draft Guidance for Industry, "Providing Regulatory Submissions in Electronic Format – Content of Labeling" published on February 5, 2004. Bayer BP supports providing to FDA labeling content in electronic format. This tool has potential to assist the pharmaceutical industry and the FDA, by improving communication and format of labeling content to the public. Additionally, Bayer BP welcomes labeling content in electronic format as an improvement to the review and approval process for new labeling and labeling changes.

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We have reviewed this draft guidance and have the following comments:

Bayer BP believes the April 5, 2004, deadline to submit comments on this draft guidance does not allow the regulated community enough time to understand the full impact on business practices. Therefore, Bayer BP requests that the comment period be extended for at least an additional eight weeks, until May 24, 2004. The extended comment period will allow Bayer BP and others the time necessary to conduct the required cost analysis of hardware, software, and personnel resources required to support the Clinical Document Architecture (CDA) in extensible markup language (XML) (i.e. Structured Product Labeling (SPL)).

In the time we have had to review the draft guidance, we have found the following items that present challenges toward implementation. Because of the extensive preparation that would be required to implement the SPL standard, Bayer BP believes the FDA's intention to change to the SPL standard for content of labeling submissions by the end of the 2004 is not feasible. The budget for the 2004 operational year has been established and implemented without making any provision for implementing the SPL standard. According to the Final Rule, published in the Federal Register (FR Vol. 68, No. 238, December 11, 2003), 21 CFR, Parts 314 and 601 require electronic submission of the content of labeling. The Rule states, "Electronic format submissions must be in a form that FDA can process, review, and

archive. FDA will periodically issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files)." In Section II of FR Vol. 68, No. 238, "At this time, portable document format (PDF) is the only type of electronic file format that we have the ability to accept for processing, reviewing, and archiving.... Software to convert electronic files to PDF is commercially available at a cost of approximately \$100 to \$300." Bayer BP will plan to submit labeling content to FDA in PDF by the effective date of June 8, 2004. However, as the guidance document unexpectedly proposes use of a new technology for processing labeling and labeling changes, Bayer BP needs additional time to assess the economic and technological impact that the CDA and XML format would have to our business.

To implement the new standard proposed in the draft Guidance, Bayer BP must take the following actions:

- Review and select hardware and software vendor – identification, analysis, contracting, installation, validation, and implementation including upgrades and/or additions to our electronic systems
- Review current business practices - impact analysis, modification planning, and implementation of existing labeling content in new format
- Establish management and control of these systems through written procedures and personnel training

Bayer BP requests the delay of the effective date to late 2005 to allow Bayer BP and the rest of the regulated community time for the necessary fiscal planning and business practice changes needed to implement such a program.

Bayer BP has comments on how the text of the draft guidance can be improved, specifically in the following two areas:

1. Section III. A. - File Formats for Providing Content of Labeling, the first sentence (line 115) should be revised to reflect the intent of the FDA to no longer accept PDF file format once the SPL format transition is complete. In the previous section II. B, New Technology for Processing Labeling and Labeling Changes, it is suggested the CDA and XML systems are proposed and not required. This clarification is key to business planning for regulatory activities involving labeling.
2. Section III. B. - Creating the Content of Labeling File is too vague. The URL provided in the draft guidance for the SPL specifications (line 127) leads to a zip file with multiple attached files within the Health Level 7 (HL7) website. The draft guidance should provide direction on how to interpret the information found at that URL. For example, there is no guidance on the 90-page document titled "Structure Product Labeling, Release 1.0, Draft Standard for Trial Use Ballot – December 2003". Guidance from the FDA on using the SPL standard, especially if a 2004 implementation date is enforced, is critical. Furthermore, this referenced SPL standard is also in draft form, and it is unclear if our comments should also be provided on this document. The level of detail and technical aspects of the SPL document would require additional time and experts within Bayer BP to assess impact and provide feedback to FDA. In addition, the draft status of the HL7 documentation indicates the XML format is an unproven technology in the area of labeling.

In summary, Bayer BP has reviewed the draft guidance document and acknowledges there will be a requirement to provide labeling content in electronic format, specifically PDF, effective June 8, 2004. Since this new rule and draft guidance are now requiring for the first time that labeling submissions be provided to FDA electronically, Bayer BP believes a 6 months time period for the transition from PDF (required as of June 8, 2004) to a new technology (end of 2004) is insufficient. Bayer BP will be revising our internal systems and procedures to adapt to the PDF requirement. The significance of moving to a completely new technology may have a potential to impact multiple areas within our organization and we will need ample time to properly plan and implement these changes into our current systems. With any new requirement, there needs to be time to assess the effectiveness of the PDF format before requiring new technology to be utilized as a new submission format.

Thank you for the opportunity to provide these comments on the draft guidance "Providing Regulatory Submissions in Electronic Format - Content of Labeling".

Sincerely,

A handwritten signature in black ink, appearing to read "Carol M. Moore", with a long horizontal flourish extending to the right.

Carol M. Moore  
Vice President  
Worldwide Regulatory Affairs  
Responsible Head/Agent

CMM/EM/AA

**Bayer HealthCare**  
**Biological Products Division**



Date: 5 April 2004

To: Dr. Robert Yetter, FDA, CBER

Fax: 301 827 9434 Pages 4

From: Audrey E. Anderson

Fax: 510.705.5553 Phone: 510.705.4174

Subject: Comments – Draft Guidance – “Providing Regulatory Submission  
in Electronic Format – Content of Labeling”

Dear Dr. Yetter:

Following this cover sheet are comments to the draft guidance titled  
“Providing Regulatory Submission in Electronic Format – Content of  
Labeling”.

Regards,  
Audrey E. Anderson

April 5, 2004

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